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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/075,079	05/08/2002	Jasbir S. Seehra	GI-5324 C1	7974

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Steven R. Eck
Five Giralda Farms
Madison, NJ 07940

EXAMINER	
WRIGHT, SONYA N	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 12/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/075,079	SEEHRA ET AL.	
	Examiner	Art Unit	
	Sonya Wright	1626	

-- The MAILING DATE of this communicati n appears on the cover sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *97* is/are allowed.

6)☒ Claim(s) *95 and 96* is/are rejected.

7)☒ Claim(s) *1-94* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-95 are pending in this application.

Election/Restrictions

Applicants' election with traverse of the compound of Example 1 of the specification, 4-({3-chloro-5-[(cyclopentylcarbonyl)amino]-2-[(phenylethylsulfanyl)methyl]-1H-indol-1-yl}methyl)benzoic acid, in the paper filed September 8, 2003, is acknowledged. No reasons have been given for traversal.

In view of Applicants' species election, the following generic embodiment has been identified for examination: R1 is R7-C(O)-N(R6)- where R6 is H and R7 is C3-C5 cycloalkyl, or phenyl, each of these rings being optionally substituted by from 1 to 3 substituents selected from halogen, C1-C6 alkyl, C1-C6 alkoxy, -NH2, -NO2, -CF3, CO2H, or –OH; R2 is as defined; R3 is as defined; R4 is selected from the group of C1-C6 lower alkyl, C1-C6 lower alkoxy, -(CH2)n-C3-C6 cycloalkyl, -(CH2)n-S-(CH2)n-C3-C5 cycloalkyl, -(CH2)n-O-(CH2)n-C3-C5 cycloalkyl, or group a); and R5 is –CH2-phenyl(R8)(R9)(R10) where R8 is COOH and R9 and R10 are both H. The remaining subject matter of claims 1-94 is withdrawn from further consideration under 37 CFR 1.142(b) as constituting other patentably distinct inventions.

The non-elected subject matter of claims 1-94 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

The withdrawn subject matter of claims 1-94 is properly restricted as said subject matter differs in structure and element from the elected subject matter so as to be

patentably distinct therefrom, i.e. a reference which anticipated the elected subject matter would not even render obvious the withdrawn subject matter and fields of search are not co-extensive.

Claims 1-94 are objected to as containing non-elected subject matter. This objection may be overcome by limiting the claims to the elected subject matter identified supra.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 95 and 96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

For rejections under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988)):

1) Nature of invention.

2) State of prior art.

3) Level of ordinary skill in the art.

4) Level of predictability in the art

5) Amount of direction and guidance provided by the inventor.

6) Existence of working examples.

7)Breadth of claims.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

1) Nature of the invention.

Claim 95 is drawn to a method of inhibiting the phospholipase activity of an enzyme. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

2) State of the prior art.

According to the specification, the prior arts teach that the direct inhibition of the activity of PLA2 has been suggested as a useful mechanism for a therapeutic agent, i.e., to interfere with the inflammatory response (e.g. J. Chang et al., Biochem.

Pharmacol., 36:2429-2436 (1987)). See the specification, page 2, lines 27-29. However, the prior arts do not indicate that the instant compound is useful in treating all forms of diseases that relate to inhibition of phospholipase activity.

3) Level of ordinary skill in the art.

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the instant compound for inhibition of phospholipase activity.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

4) Level of predictability in the art.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. One of skill in the

art is unable to fully predict possible results from the administration of the instant compounds due to the unpredictability of the art pertaining to phospholipase activity.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

5) Amount of direction and guidance provided by the inventor.

Applicant provides limited guidance regarding the use of the instant compounds in the inhibition of phospholipase activity. Applicants state that a reaction catalyzed by PLA2 is believed to represent the rate-limiting step in the process of lipid mediated biosynthesis and the production of inflammatory prostaglandins and leukotrienes. See the specification, page 2, lines 8-12. Applicant states that it would be desirable to identify chemical inhibitors of the action of enzymes which inhibitors could be used to treat inflammatory conditions. See the specification, page 4, lines 18-21. The guidance is limited because various forms of diseases related to phospholipase inhibition have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol.

6) Existence of working examples.

Applicant provides working examples of inhibition in the LysoPC Assay in Table 1 on pages 163-169. Applicant provides working examples of inhibition in the rat CPE

model on pages 170. However, the limited examples do not provide sufficient evidence to support a broad claim drawn to inhibiting phospholipase activity.

7) Breadth of claims.

Claim 95 is extremely broad due to the large number of diseases related to the inhibition of phospholipase activity of an enzyme. Applicant has not provided sufficient evidence to support a claim drawn to inhibiting the phospholipase activity of an enzyme in all possible occurrences.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

In view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test how the instant compound is useful in the inhibition of phospholipase activity with no assurance of success.

1) Nature of the invention.

Claim 96 is directed to a method of treating an inflammatory response in a mmammalian subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

2) State of the prior art.

According to the specification, the prior arts teach that the direct inhibition of the activity of PLA2 has been suggested as a useful mechanism for a therapeutic agent, i.e., to interfere with the inflammatory response (e.g. J. Chang et al., Biochem. Pharmacol., 36:2429-2436 (1987)). See the specification, page 2, lines 27-29. However, the prior arts do not indicate that the instant compound is useful in treating all forms of inflammatory response.

3) Level of ordinary skill in the art.

The level of skill in the art is high. Due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant compound in treating inflammatory response.

Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search , but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

4) Level of predictability in the art.

The art pertaining to inflammatory response remains highly unpredictable. The various forms of these disorders have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. One of skill in the art is unable to fully predict possible results from the administration of the instant compounds due to the unpredictability of the art pertaining to phospholipase activity.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

5) Amount of direction and guidance provided by the inventor.

In terms of guidance, the limited background information of pages 1-4 lacks sufficient enablement for the claimed scope with regard to treating inflammatory response. Applicant provides examples of inflammatory responses on page 99, lines 25-29. However, the examples of inflammatory responses do not enable the full scope of the claim.

6) Existence of working examples.

The term "treating inflammatory response" includes a large number of disorders. Applicant provides no working examples of how the instant compound is used to treat inflammatory response.

7) Breadth of claims.

The claims are extremely broad because the method of claim 96 encompasses treatment of all forms of inflammatory response.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The specification did not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with this claim. In particular, the specification failed to enable the skilled artisan to practice the invention without undue experimentation. The skilled artisan would have a numerous amount of modifications to perform in order to use compound as claimed.

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not perform the claimed method of use without undue experimentation.

In order to overcome the rejections of claims 95 and 96, it is suggested that Applicants cancel claim 95 and limit claim 96 to the following diseases which are shown on page 99, lines 26-29: rheumatoid arthritis, psoriasis, asthma, inflammatory bowel disease, osteoporosis, colitis, myelogenous leukemia, diabetes, and atherosclerosis.

Remarks

The continuing data at the beginning of the specification is not consistent with the continuing data in the Patent Office records. It is requested that Applicants verify that the continuing data at the continuing data at the beginning of the specification is correct.

The reference cited on the PTO-892 is included only to show the state of the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sonya Wright, whose telephone number is (703) 308-4539. The examiner can normally be reached on Monday-Friday from 8:00 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (703) 308-4537. The Unofficial fax phone number for this Group is (703) 308-7922. The Official fax phone numbers for this Group are (703) 308-4556 or 305-3592.

When filing a FAX in Technology Center 1600, please indicate in the Header (upper right) "Official" for papers that are to be entered into the file, and "Unofficial" for draft documents and other communications with the PTO that are not for entry into the file of the application. This will expedite processing of your papers.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [joseph.mckane@uspto.gov]. All Internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via Internet e-mail where sensitive data will be exchanged

or where there exists a possibility that sensitive data could be identified unless there is of record an express waiver of the confidentiality requirements under 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published by the Patent and Trademark Office Official Gazette on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-1235.

for Robert W. Ramsuer

Joseph K. McKane

Supervisory Patent Examiner

Group 1600

Sonya Wright

November 24, 2003